Be-FAST: A spatial epidemiological model for between- and within-farms disease spread. Application to Classical Swine Fever.

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Collaborations:

Outlines

- A short introduction to epidemiology
  -Basic concepts
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- Classical Swine Fever description
  -Disease description
  -Control measures
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- Be-FAST model
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  -Individual based model
- Numerical experiments
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  -Results
  -Comparison with InterSpread/Real cases

Part I: A short introduction to epidemiology

Basic definition

The epidemiology is the study of the distribution and determinants of prevalence (i.e., affected people) of the diseases in humans or animals (veterinarian).

The main objectives of this discipline are:

- Describe the distribution (i.e., where? when? How many?) of a disease. In particular, to know if the outbreak will be endemic (i.e., does not disappear) or not.
- Identify the risk factors or determinants (i.e., causes of infection) in order to explain the non-uniformity.
- Preventive role: Plan, implement and evaluate detection, control and prevention programs.

Here, we focus on the epidemiological modelling: Mathematical models that simulate the spatial and temporal evolution of a disease outbreak.

Historical context

Some important historical results:

- 1760 - Daniel Bernouilli: a first mathematical model to study the efficiency of the smallpox virus variolation in healthy people in Turkey.
- 1906 - William Heaton Hamer: a discrete time model to explain the recurrence of measles (Sarampion) epidemics in England: introduce a dependence between the disease incidence and the product of the densities of the susceptible (non-contaminated) and infective.
- 1911 - Ronald Ross: PDE model to study the link between malaria and mosquitoes: help to eradicate this disease in Europe.
- 1926 - Mc Kendrick and Kermack: demonstrate that density of susceptible must exceed a critical value in order for an epidemic outbreak to occur.

Historical context

Currently the number of model is widely increasing in order to study the actual important diseases:

- New diseases: S.R.A.S., Influenza, HIV...
- Re-emergent diseases: Malaria, Syphilis, Tuberculosis...

Those models are based on various mathematical tools: Dynamical systems, PDE, Montecarlo algorithms, Networks, Markov processes,...

Furthermore, they are complex and can now take into account various disease properties such as: passive immunity, gradual loss of immunity, stages of infection, disease vectors, age structure, mixing groups, spatial spread, vaccination, quarantine...

Disease classification

agent	person→person	person→environment environment→person	reservoir→vector vector→person	reservoir→person
virus	measles chickenpox mumps rubella smallpox influenza poliomyelitis herpes HIV (AIDS virus) SARS (coronavirus)		arboviruses: yellow fever dengue fever encephalitis tick fever sandfly fever West Nile virus	rabies hantavirus
bacteria	gonorrhea tuberculosis pneumonia meningitis strep throat pertussis	typhoid fever cholera Legionnaire's disease	plague lyme disease	brucellosis tuleramia anthrax
protozoa	syphillis	amebiasis	malaria trypanosomiasis leishmaniasis	
helminths (worms)		dracunculiasis	schistomosomiasis filariasis onchocerchiasis	trichinosis
prions	kuru			BSE (mad cow disease) VCJD (in humans) scrapie

A classical model: S.I.R.

We briefly present one of the most used model in epidemiology: 'SIR' model.

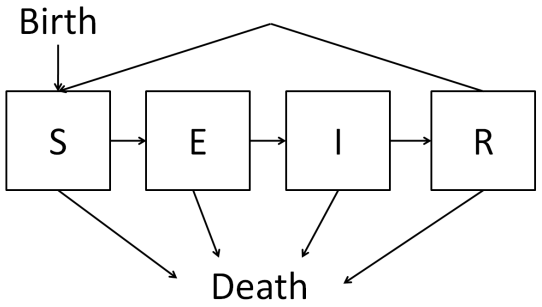
It´s a compartment model that simulate the temporal evolution of the population proportion in each compartment taking into account the flow between them.

Example: considering a virus type disease, we consider that an individual in the considered population is in one of the following compartments:

- S - Susceptible: free of disease.
- E - Infected: in latent phase, can´t infected other people.
- I - Infectious: can infected other people.
- R - Recovered: have an immunity against the disease: can´t be infected.

A classical model: S.I.R.

The diagram of the considered flow can be:



where the flows are of the forms:

- S → E: It´s of the form $\beta \frac{I(t)}{N} S(t)$, where β be the average number of adequate contacts (i.e., sufficient for transmission) of a person per unit time. This can be written as:

$$\frac{\mathrm{d}S(t)}{\mathrm{d}t} = -\beta \frac{I(t)}{N} S(t), \frac{\mathrm{d}E(t)}{\mathrm{d}t} = \beta \frac{I(t)}{N} S(t)$$

- E → I (or I → R, R → S, death and birth): a person stay during an average period of $\frac{1}{\delta}$ time units in latent phase before becoming infectious. This can be reformulated as:

$$\frac{\mathrm{d}E(t)}{\mathrm{d}t} = -\delta E(t), \frac{\mathrm{d}I(t)}{\mathrm{d}t} = \delta E(t)$$

A classical model: S.I.R.

This can be summarized by the following dynamical system:

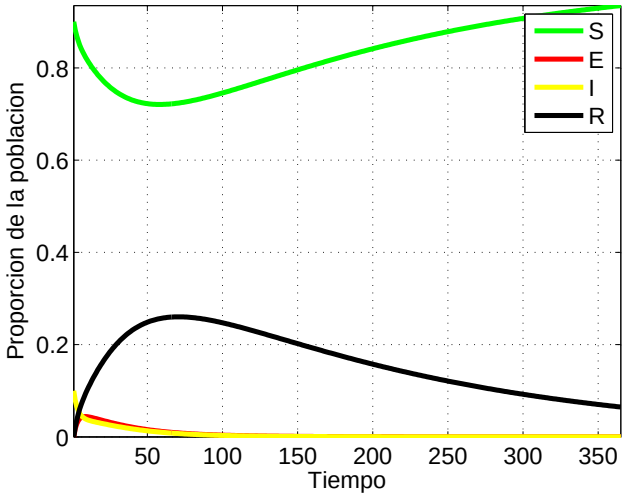
$$\begin{cases} \frac{\mathrm{d}S(t)}{\mathrm{d}t} = -\beta\frac{I(t)}{N}S(t) + \mu(E(t)+I(t)+R(t)) \\ \frac{\mathrm{d}E(t)}{\mathrm{d}t} = \beta\frac{I(t)}{N}S(t) - (\delta+\mu)E(t) \\ \frac{\mathrm{d}I(t)}{\mathrm{d}t} = \delta E(t) - (\gamma+\mu)I(t) \\ \frac{\mathrm{d}R(t)}{\mathrm{d}t} = \gamma I(t) - \mu R(t) \end{cases}$$

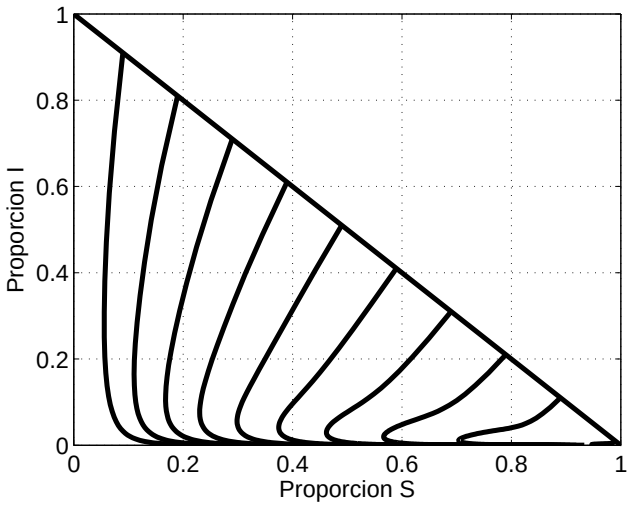
Then, we study one of those three important threshold quantity: basic reproduction number R_0 (the most used), replacement number R or contact number σ that will indicate if the outbreak is endemic or not.

In our particular case $R_0 = \frac{\beta\delta}{(\delta+\mu)(\gamma+\mu)}$ and we can proof (by linearization) that there is a globally asymptotically stable disease-free equilibrium if $R_0 \leq 1$ and there is an locally asymptotically stable endemic equilibrium when $R_0 > 1$ (if we start in a defined admissible space).

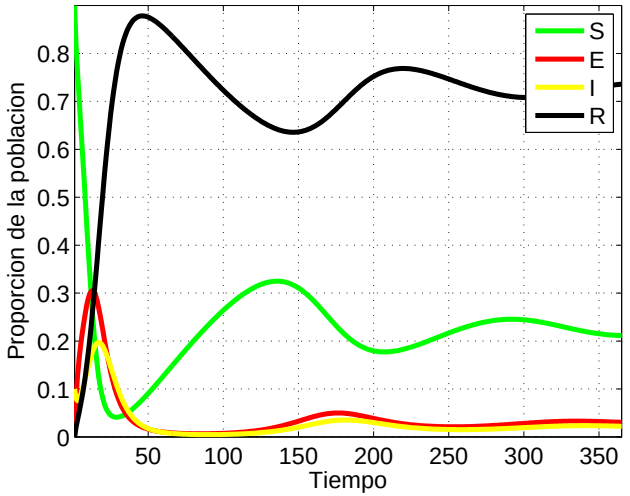
A classical model: S.I.R.

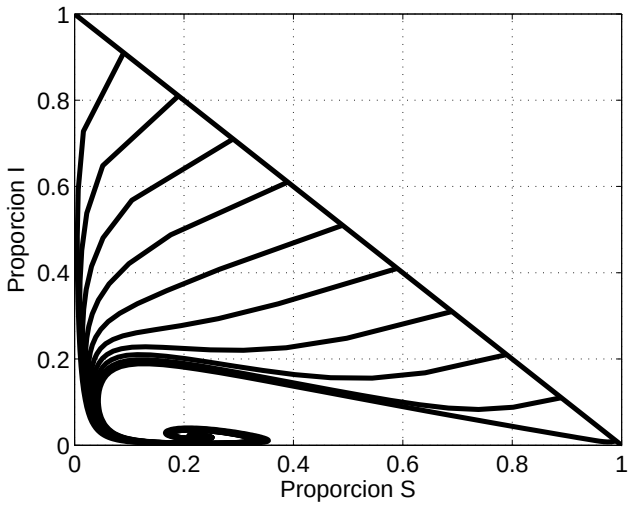
$R_0 \leq 1$





$R_0 > 1$





A classical model: S.I.R.

Advantages of the S.I.R. models:

- Computationally cheap.
- Allows to have a quick idea of the outbreak behavior.

Main drawbacks:

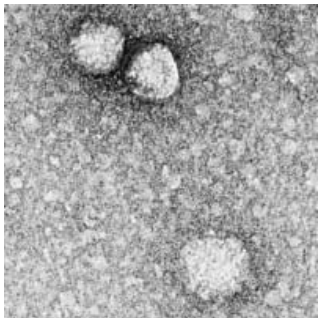
- Valid only for small spatial environments with an heterogeneous population density distribution (for instance, inside a farm).
- Don´t take into account efficiently the spatial diffusion of the outbreak (can be approximated by using a cluster structure).

Our idea: take the advantages of this technique (simulate the spread within a farm) and combine it with a more complex stochastic model (simulate the spread between farms).

Part II: Classical Swine Fever description

Disease description: Biological aspect

- Classical swine fever (CSF) is a highly contagious viral disease of domestic and wild pigs caused by a *Pestivirus*.



- Infected animals present various symptoms (fever, lesions, hemorrhages...) producing high mortality and severe economical consequences in infected regions.

Disease description: current epidemic situation

- This disease remains endemic in South and Central America, Africa and South-east of Asia.
- In Europe, it is sporadic: from 1996-2007, 8307 outbreaks reported affecting 49% of EU member states.
- Focusing on Spain (second pig producer in EU), two epidemics in 1997-1998 and 2001-2002, afected 10 provinces and more than 200.000 pigs were slaughtered.

Disease description: ways of transmission

The main known ways of transmission farm to farm has been described as:

- Movement of infected animals.
- Contact with contaminated vehicles.
- Airborne spread.
- Movement of people: yatrogenic, farmers, etc.
- Other infected fomites: food, material, etc.

Control measures

The European and Spanish legislation to control CSF epidemics are based on:

- Depopulation of detected farms.
- Zoning.
- Movement restrictions.
- Increase of active surveillance: sampling and test diagnostics, education campaigns, etc.
- Tracing.

Mathematical modeling interest

Principal objectives:

Develop a model adapted to the Spanish case (database, production type, ...) in order to evaluate the CSF spread between farms and allowing to:

- Analyze the spread patterns.
- Characterize the risk areas for disease introduction/spread.
- Evaluate the effectiveness of the control measures.
- Estimate the economic losses generated by the CSF spread (for insurance companies): WIP (with E. Fernandez Carillon).

Article associated to this work: (with D. Ngom) ***A novel spatial and stochastic model to evaluate the within and between herds transmission of classical swine fever virus: I. General concepts and description of the model.*** *and* ***II. Sensitivity analysis.*** *in* ***Veterinary microbiology*** *and* ***III. Validation.*** *in* ***ANOR****.*

Part III: Be-FAST model

General description

The Be-FAST (Between-Farm-Animal Spatial Transmission) model is based on a Monte-Carlo algorithm.

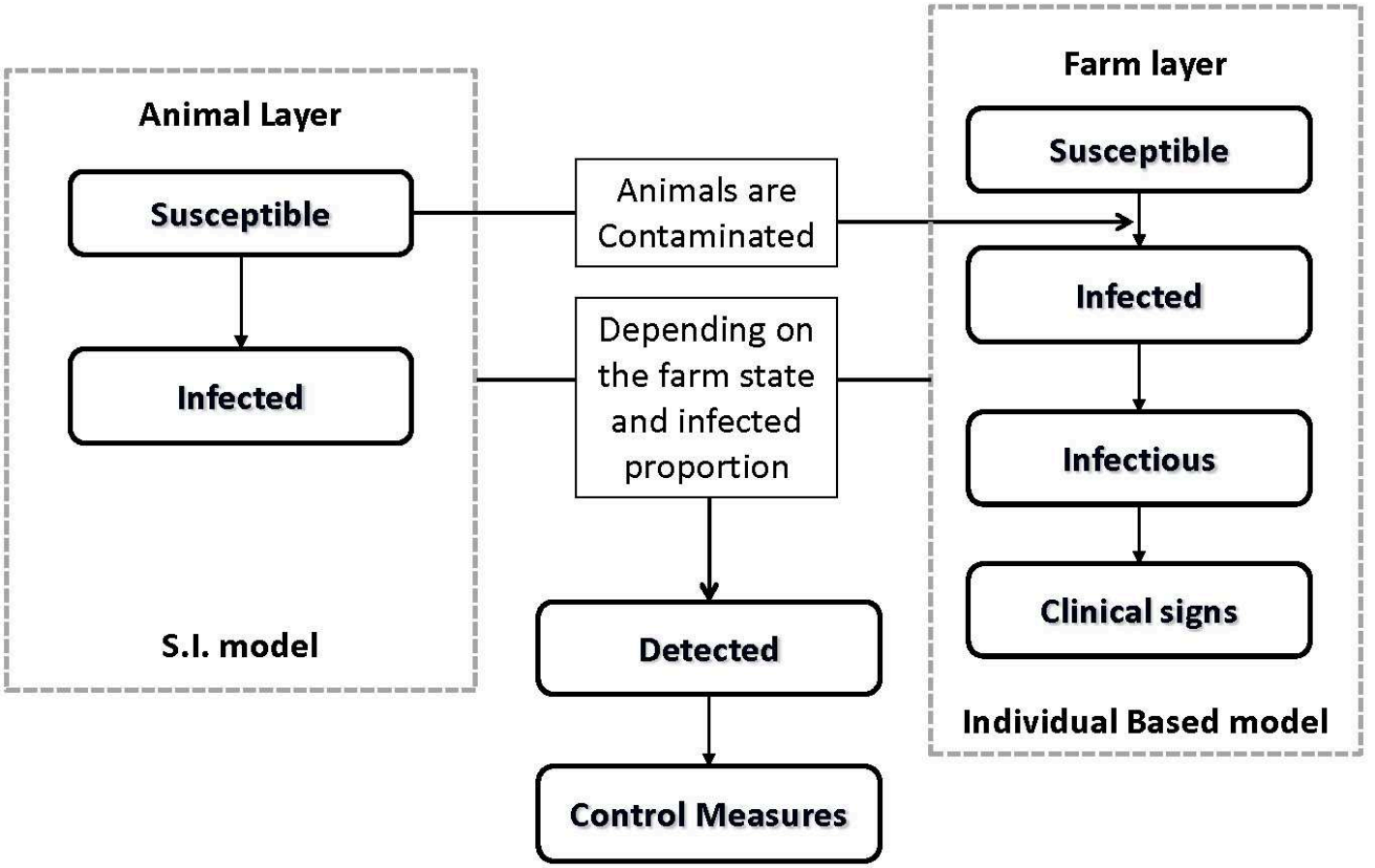
For each scenario:

- Day 1: One randomly selected farm is infected.
- During T days, within and between farm daily transmission processes are applied.

Control measures can be activated/deactivated

At the end of the simulation various output referring to risk management are analyzed.

General description



Model Inputs

Real Data:

Farm data: For each farm i we know ():

- (X_i, Y_i): geographical location
- $N_i(0)$: number of pigs
- T_i: type of production
- INT_i: integration group
- SDA_i: Sanitary Defense Association group

Shipment data: For each pig shipment:

- Farm of origin and destination
- Date of shipment
- Number of pigs shipped

Model Inputs

Other Inputs:

Parameter description	Distrib./Value	Reference
Daily transmission parameter	0.53	Klinkenberg, 02
PI due to peoples	Bernoulli(0.0065)	Stegeman, 02
Daily PD of the index case	Bernoulli(0.03)	Kartsen, 05
Daily PD due to clinical	Bernoulli(0.06)	Kartsen, 05
PD due to tracing	Bernoulli(0.95)	M.A.P.A.,08
DPD in control zone	Bernoulli(0.98)	J.C.L, 08
DPD in surveillance zone	Bernoulli(0.95)	J.C.L, 08
PR of vehicle	Bernoulli(0.95)	J.C.L, 08
Delay for depopulation	Table	Elbers, 99
Tracing period (days)	60	M.A.P.A.,08
Latent period (days)	Poisson(7)	Kartsen, 05a
Incubation period (days)	Poisson(21)	Kartsen, 05a
⋮	⋮	⋮

Within-farm transmission

The within spread of a particular farm i is modeled using a stochastic 'Susceptible-Infected' model.

More precisely:

Pigs are characterized in two states: susceptible and infected:

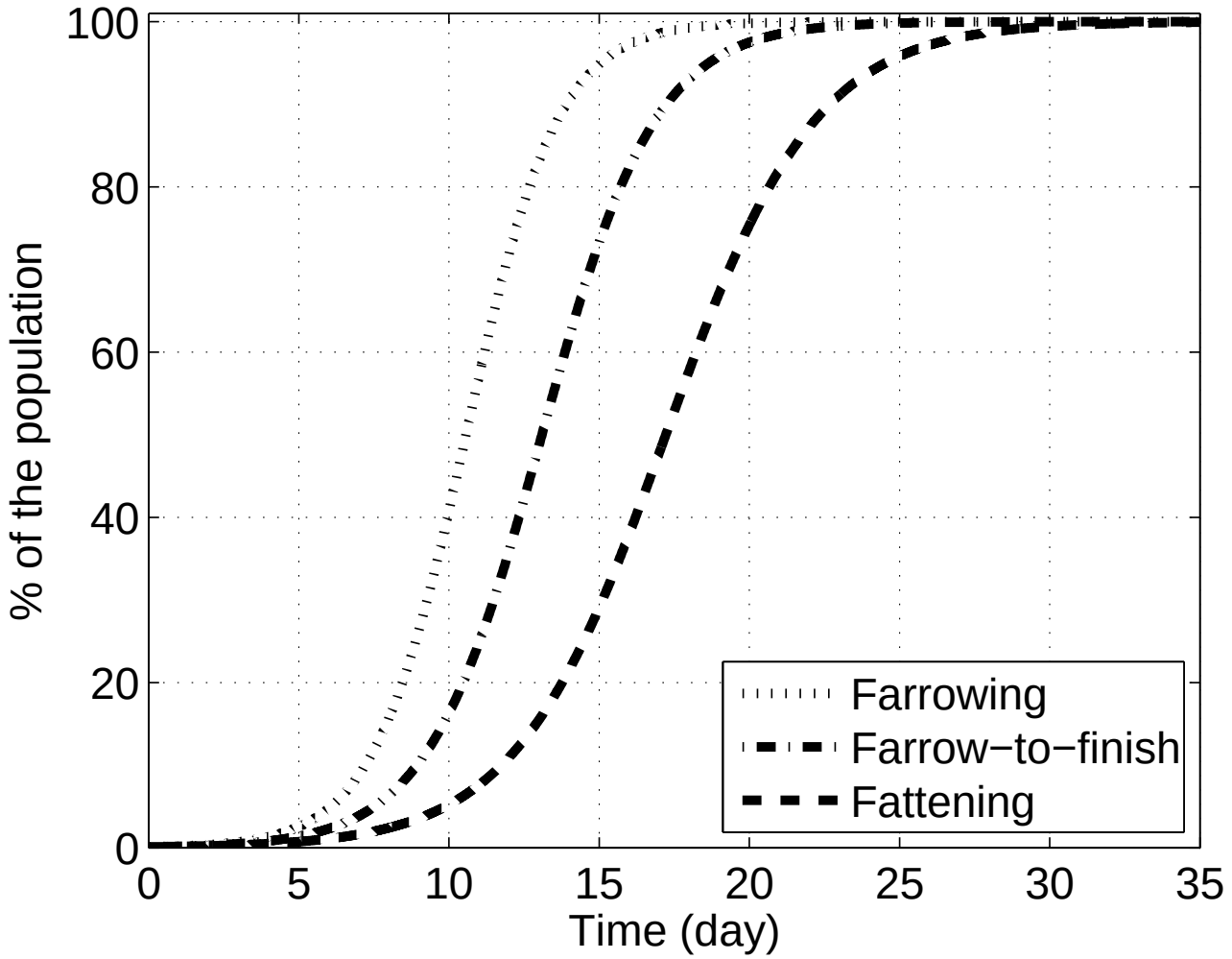
The daily evolution $S_i(t)$ and $I_i(t)$ of the number of susceptible and infected pigs at farm i at day t, is governed by:

$$S_i(t+1) = S_i(t) - P(t)$$
$$I_i(t+1) = I_i(t) + P(t)$$

where $P(t)$ follows Poisson($\beta_i \frac{S_i(t)I_i(t)}{S_i(t)+I_i(t)}$) and β_i is a known transmission parameter.

Within-farm transmission

Mean evolution depending of the herd type:



Between-farm CSF transmission

The Between-farm CSF transmission is modeled using a stochastic 'Individual Based' model:

More precisely:

Farms are characterized in four states: susceptible (S_H), infected (I_H), infectious (F_H) and clinical signs (C_H).

The order of transition from a state to the other is:

$$S_H \rightarrow I_H \rightarrow F_H \rightarrow C_H$$

Between-farm CSF transmission

Transition from ”susceptible” to ”infected”

Due to direct and indirect contacts between farms.

Those contacts are simulated using the real network data.

The probability of transmission per contact (PTC) is computed as following:

- Movement of animals: The PTC depends on the number of moved animals and $I_i(t)$ of the origin farm i.
- Movement of vehicles and people: The PTC follows Bernoulli with fixed means.
- Local spread: Occurs between a farm i in the proximity of an infected farm j. The daily PT follows Bernoulli with mean depending on $I_j(t)$ and the distance between farms.

Between-farm CSF transmission

Transition from ”infected” to ”infectious”

Depends on a latent period that follows a Poisson(7) days after the first infection in the considered farm.

Transition from ”infectious” to ”clinical signs”

Depends on an incubation period that follows a Poisson(21) days after the beginning of the infectious state in the considered farm.

Control measures

Detection of farms due to clinical signs: The probability of detection per day (PDD) follows Bernoulli with fixed means (Before/after 1st detection).

Zoning: Zones are defined around detected farms. A movement restrictions is applied to zoned farms during an Overlapped period and follows Bernoulli with fixed means. The PDD follows Bernoulli($\gamma \frac{I_i(t)}{S_i(t)+I_i(t)}$) with γ depending on the zone type.

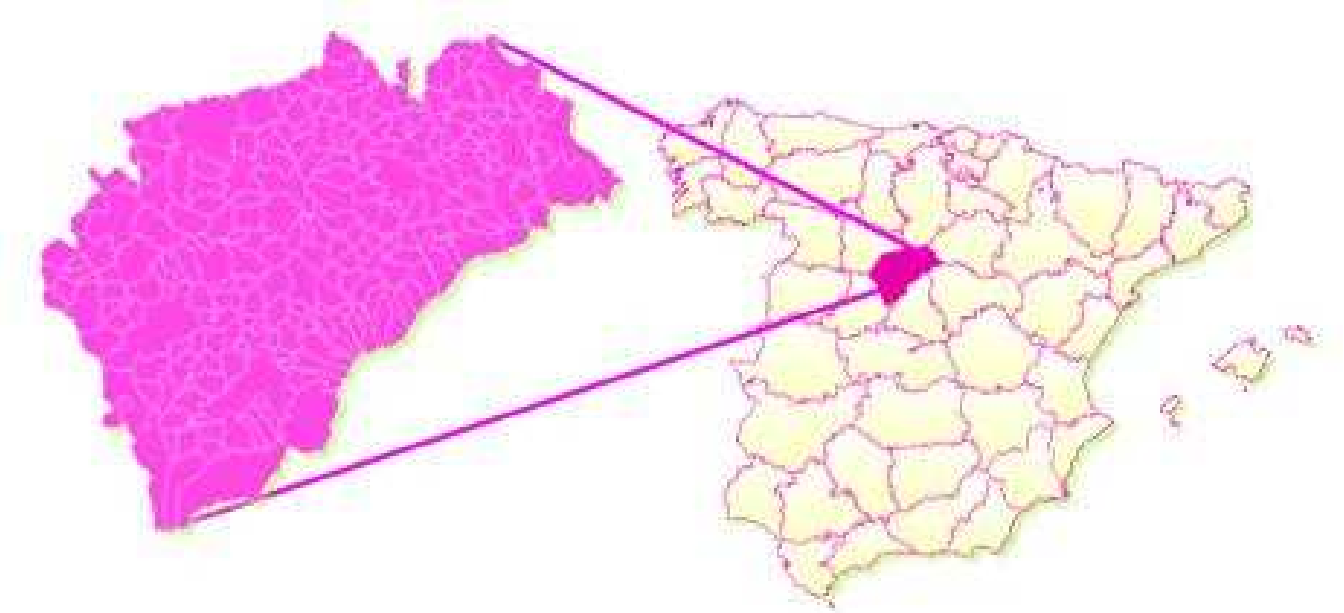
General movement restrictions: After each detection and during 90 days, all movements are restricted following Bernoulli with fixed mean.

Tracing: Trace the contacts of a detected farm 60 days before detection. The probability of tracing movements and PDD follow Bernoulli with fixed mean.

Part IV: Numerical experiments

Region and data

We consider the Spanish region of Segovia (important areas of pig production) with CSF outbreaks in 1997-1998 (Data used for validation).



We use real data provided by:

MINISTERIO DE MEDIO AMBIENTE Y MEDIO RURAL Y MARINO

Junta de Castilla y León

In 2008: 1.417 pig herds; 1.403.800 pigs; 10.046 shipments.

Region and data

Farm data:

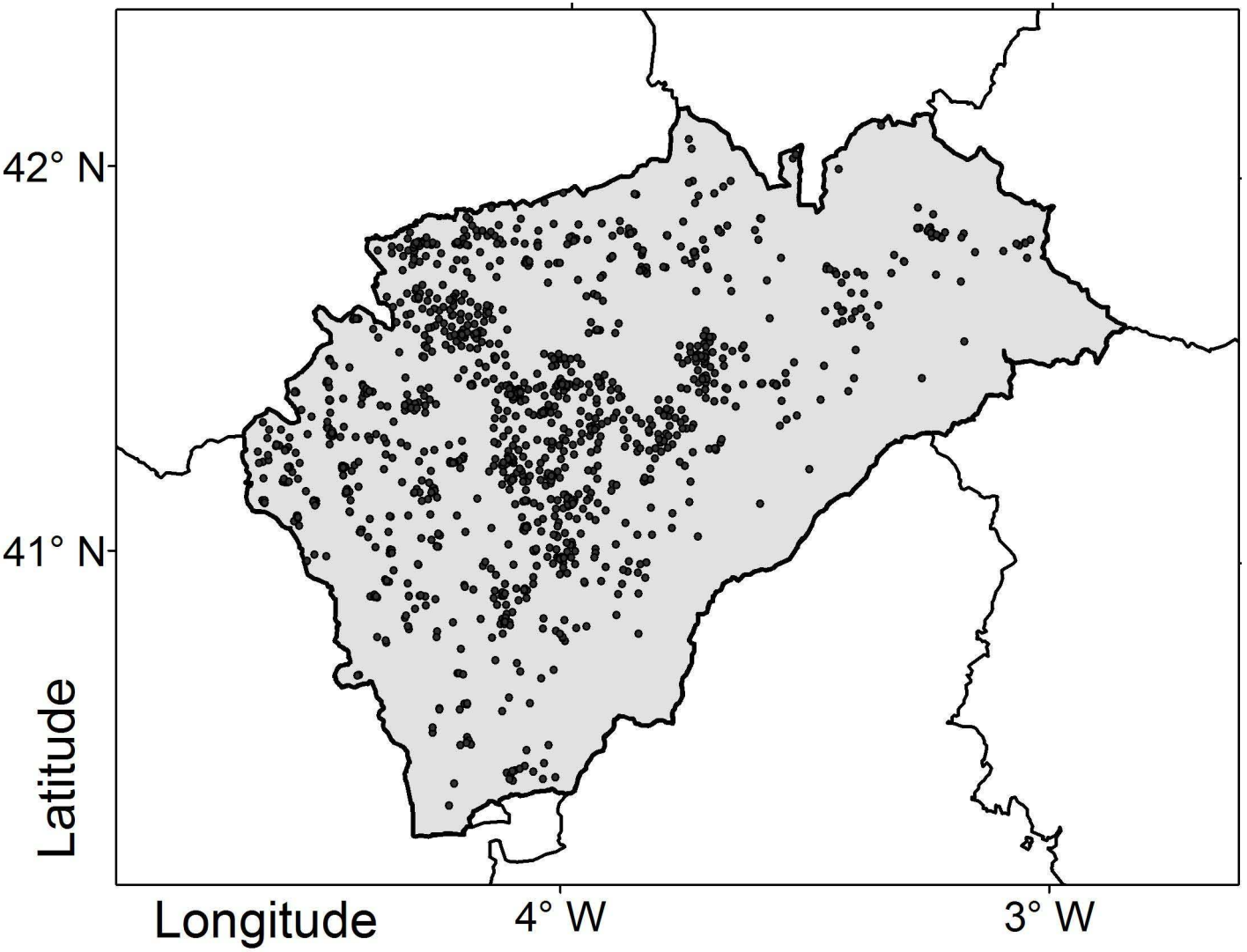
	A	B	C	D	E	F	G
1	A_CEA	PORCINO	CENSO_PORCINO	INTEG_PORCINO	ADS_PORCINO	LONGITUD_PORCINO	LATITUD_PORCINO
2	ES400060200011	Cebo	300	60218674	0840200004	-3,7915418	41,244351
3	ES400140220011	Cebo	1100	40052599	0840200026	-3,7767965	41,5294636
4	ES400160200091	Cebo	1428	60218674	0840200026	-3,7035766	41,3094811
5	ES400160220051	Producción de ciclo cerrado	920	60218674	0840200026	-3,693445	41,313104
6	ES400250220131	Producción mixto	1402	60218674	0840200026	-3,6520647	41,3181521
7	ES400390220051	Cebo	2184	60218674	0840200004	-3,5389075	41,4526753
8	ES400400220011	Cebo	800	40052599	0840200021	-3,9310925	41,2813726
9	ES400400220221	Cebo	220	40052599	0840200021	-3,9301012	41,2637932
10	ES400400220241	Cebo	220	40052599	0840200021	-3,930076	41,2637565
11	ES400400220551	Cebo	1700	60218674	0840200021	-3,976733	41,2634155
12	ES400400220581	Cebo	2000	60218674	0840200021	-3,9369386	41,2653142
13	ES400400220671	Cebo	750	60218674	0840200021	-3,9683618	41,2557336
14	ES400400220731	Producción de lechones	3089	60218674	0840200025	-3,859745	41,2639919
15	ES400440220031	Cebo	624	40052599	0840200002	-3,8924685	41,3675769
16	ES400470000001	Producción de lechones	670	40052599	0840200002	-3,8399159	41,4177965

Shipment data:

	A	B	C	D	E
1	A_CEA_ORIG	A_CEA_DEST	ESPECIE	F_EXPEDICION	ANIMS
2	ES401000220241	ES400410220291	CERDOS	02/01/2008	68
3	ES401000200111	ES401742000011	CERDOS	02/01/2008	22
4	ES400910220001	ES402250220071	CERDOS	07/01/2008	88
5	ES401190220071	ES401120220031	CERDOS	03/01/2008	22
6	ES400030220081	ES402250220071	CERDOS	09/01/2008	33
7	ES401000200111	ES401742000011	CERDOS	14/01/2008	17

Region and data

Farm distribution:



Considered experiments

We have considered two experiments:

- **WM**: Without control measure and $T = 200$ days.
- **AM**: All control measures activated/run until the epidemic end.

We use a MatLab implementation of our model **BF** and a Pentium 4 of 3.4Ghz with 2Gb: 14500 sec for **AM** and 28000 sec for **WM** considering 1000 scenarios.

Model comparison: Same experiments have been performed by using **InterSpread IS** (Main differences: without SIR / difficulty to use real database).

Sensitivity analysis: Model was demonstrated to be robust to various SA experiments (not presented here).

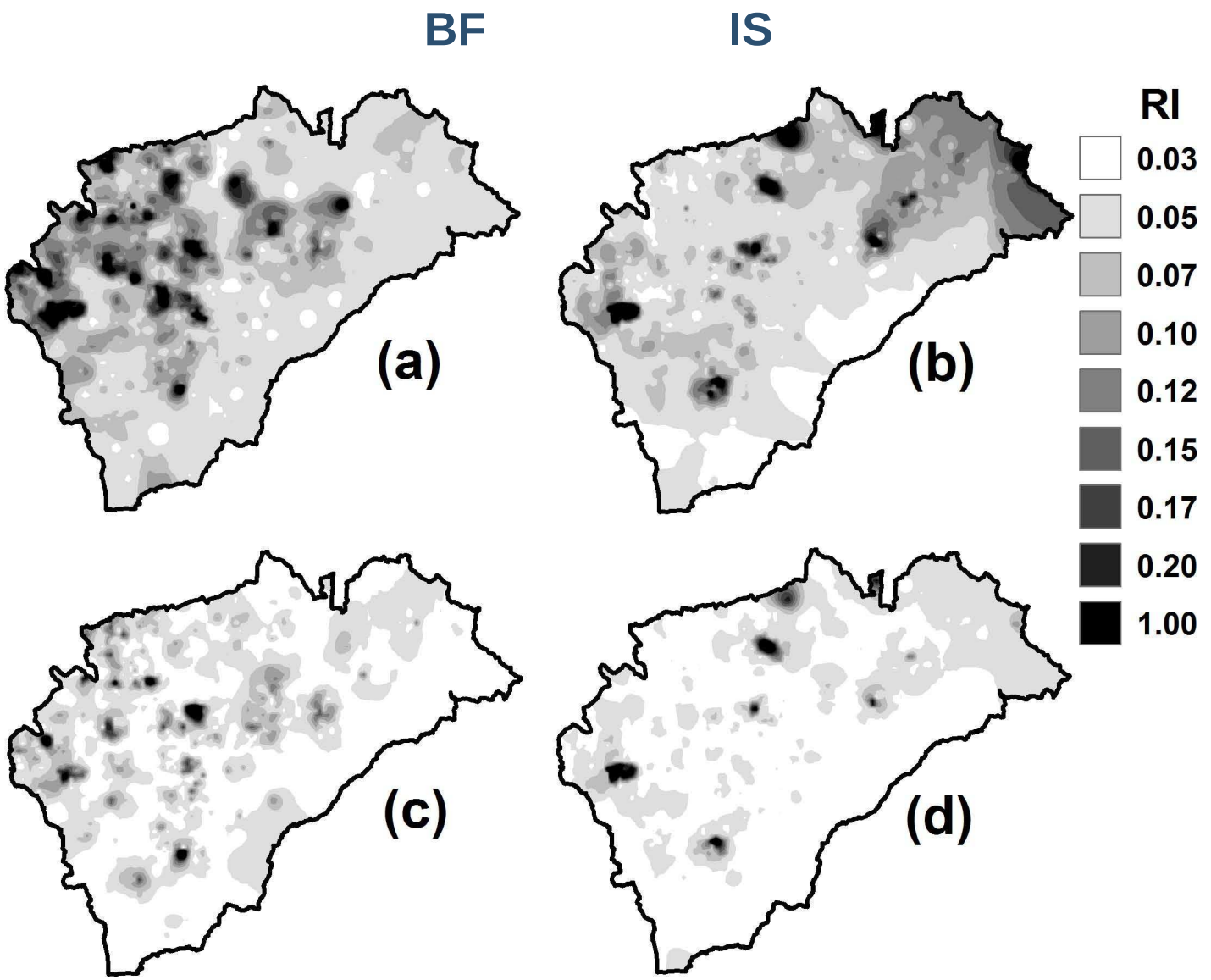
Scenario example without measure

Scenario example with measures

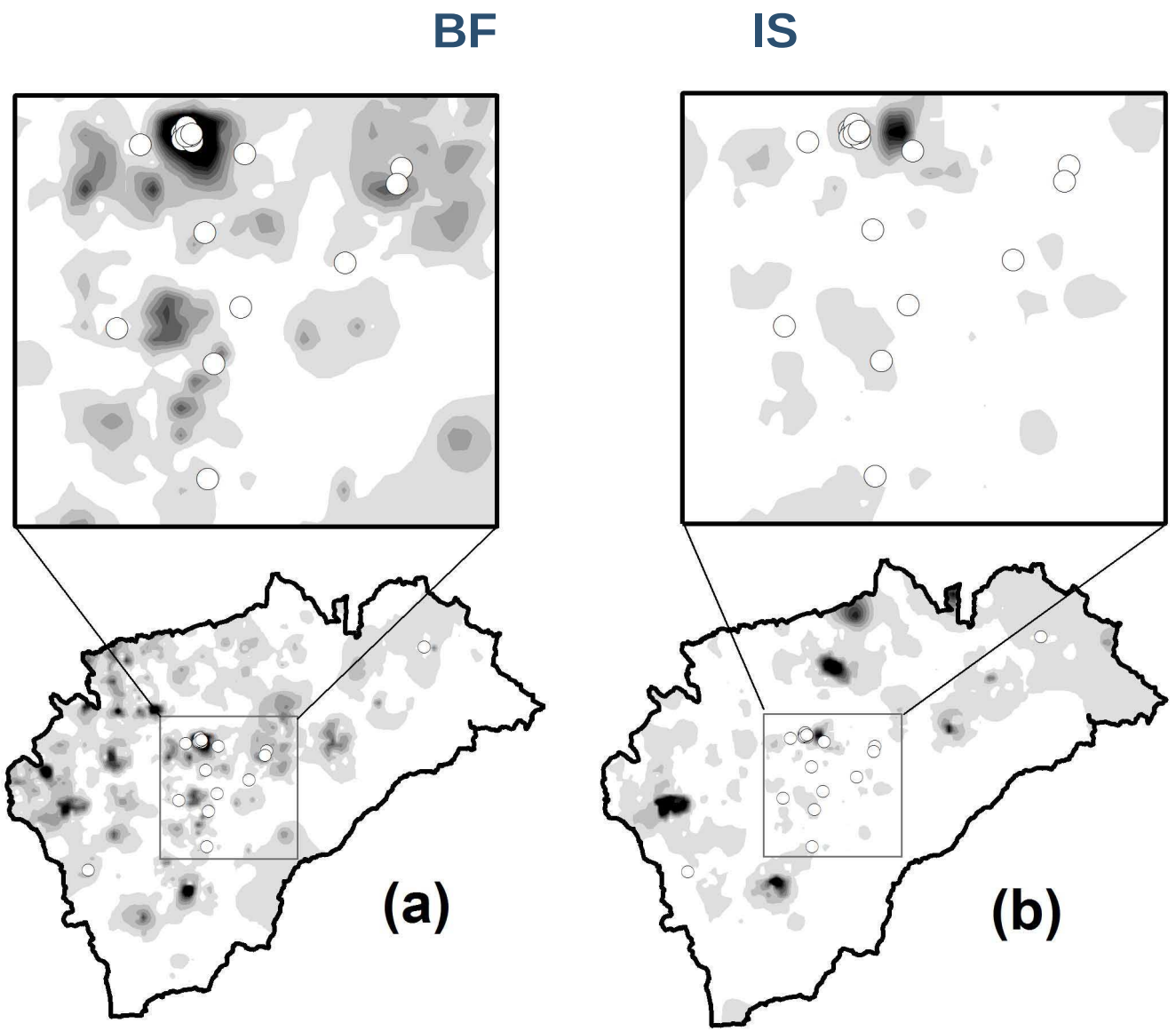
Results

Scenario	WM		AM		Real
Output	**BF**	**IS**	**BF**	**IS**	**-**
Mean number of Infected farms	32	58	3.3	4.6	22
Mean duration in days	-	-	63	78	57
% Infections due to local spread	54	51	64	61	52
% Infections due to people	14	10	9	5	16
% Infections due to vehicle	26	13	17	10	25
% Infections due to pig transport	6	26	10	24	7
% Detections due to clinical sign	-	-	47	38	44
% Detections due to zoning	-	-	30	50	28
% Detections tracing	-	-	23	12	28

Risk map



Validation considering the 1997-98 outbreak



Conclusions and perspectives

Conclusions and perspectives

Conclusions:

We have introduced and described a new model for the study of CSF spread.

- Novel characteristics respecting to other models: Hybrid model, use of real database $\Rightarrow$ interest for risk maps.
- The results are consistent with other models: here, InterSpread but also: Karsten et al., Jalvingh et al. and Saatkamp et al.

Next steps: Work In Progress (with E. Fernandez Carillon)

- Include the economical aspect.
- Applications to risk management: Optimization of new control measures.
- Extension to other diseases.

Conclusions and perspectives

!!! Thank you for your attention!!!

!!! MATHS + VETS = SUCCESS !!!